

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-119. (Canceled)

120. (Currently amended) A chemically stable antioxidant compound, comprising:

a lipophilic cationic moiety linked by a linking moiety to an antioxidant moiety;

and

an anionic complement for said cationic moiety,

wherein the cationic moiety is capable of mitochondrially targeting the antioxidant moiety, ~~and~~ wherein the anionic complement is a pharmaceutically acceptable anion that is not a halogen ion or a nitrate anion and is selected from the group consisting of an alkyl sulfonate, an aryl sulfonate, tetrafluoroborate, trifluoromethanesulfonate, hexafluoroantimonate, hexafluoroarsenate, hexafluorophosphate, tetraphenylborate, and tetra(perfluorophenyl)borate, and does not exhibit reactivity against the antioxidant moiety, the cationic moiety or the linking moiety, and wherein the antioxidant compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity.

121. (Previously presented) A compound according to claim 120 wherein the lipophilic cationic moiety is a substituted or an unsubstituted triphenylphosphonium cation.

122. (Previously presented) The compound of claim 120 wherein the pharmaceutically acceptable anion is not a halogen ion.

123. (Previously presented) The compound of claim 120 wherein the pharmaceutically acceptable anion is not nucleophilic.

124. (Previously presented) The compound of claim 120 wherein the pharmaceutically acceptable anion is an alkyl sulfonate.

125. (Previously presented) The compound of claim 120 wherein the pharmaceutically acceptable anion is selected from the group consisting of methanesulfonate, p-toluenesulfonate, ethanesulfonate, benzenesulfonate and 2-naphthalenesulfonate.

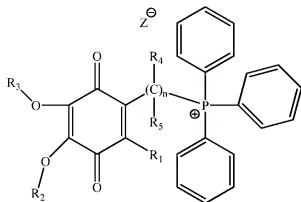
126. (Previously presented) The compound of claim 120 wherein the pharmaceutically acceptable anion is methanesulfonate.

127. (Previously presented) A compound according to claim 120 wherein the antioxidant moiety is a quinone or a quinol.

128. (Previously presented) A compound according to claim 120 wherein the antioxidant moiety is selected from the group consisting of (i) vitamin E (ii) a chain breaking antioxidant, (iii) a fullerene, and (iv) a spin trap.

129. (Previously presented) A compound according to claim 120 wherein the antioxidant moiety is selected from the group consisting of butylated hydroxyanisole, butylated hydroxytoluene, 5,5-dimethylpyrroline-*N*-oxide, *tert*-butylnitrosobenzene, *tert*-nitrosobenzene and α -phenyl-*tert*-butylnitron.

130. (Previously presented) A compound according to claim 120 having the general formula I:



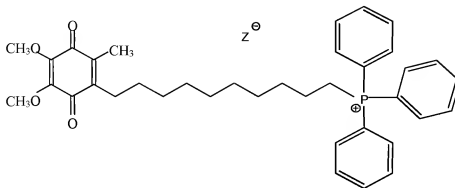
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or its quinol form, wherein R_1 , R_2 , and R_3 are the same or different and are selected from C_1 to C_5 alkyl, substituted C_1 to C_5 alkyl and H, wherein R_4 and R_5 are independently selected from the group consisting of H, hydroxyl, carboxyl, amide, unsubstituted or substituted alkyl, unsubstituted or substituted alkenyl and unsubstituted or substituted alkynyl, and wherein n is an integer from 2 to 20, and wherein Z is the anionic complement.

131. (Previously presented) A compound according to claim 130 wherein Z is selected from the group consisting of an alkyl sulfonate and an aryl sulfonate.

132. (Currently amended) A compound according to claim 130 wherein C of $H(C)_n$ is saturated.

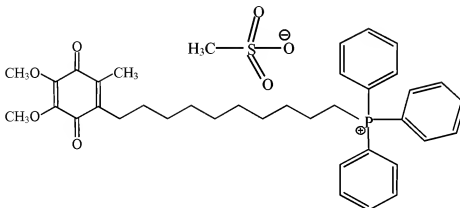
133. (Previously presented) A compound according to claim 120 having the formula:



II

or its quinol form, wherein Z is the anionic complement.

134. (Previously presented) A compound according to claim 120 having the formula:



(III)

or its quinol form.

135. (Currently amended) A pharmaceutical composition, comprising:
a chemically stable antioxidant compound that comprises a lipophilic cationic moiety linked by a linking moiety to an antioxidant moiety;

an anionic complement for said cationic moiety, wherein the cationic moiety is capable of mitochondrially targeting the antioxidant moiety, ~~and~~ wherein the anionic complement is a pharmaceutically acceptable anion that is not a halogen ion or a nitrate anion and is selected from the group consisting of an alkyl sulfonate, an aryl sulfonate, tetrafluoroborate, trifluoromethanesulfonate, hexafluoroantimonate, hexafluoroarsenate, hexafluorophosphate, tetraphenylborate, and tetra(perfluorophenyl)borate, and does not exhibit reactivity against the antioxidant moiety, the cationic moiety or the linking moiety, and wherein the antioxidant compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity; and a carrier or excipient.

136. (Previously presented) The pharmaceutical composition of claim 135 wherein the lipophilic cationic moiety is a substituted or an unsubstituted triphenylphosphonium cation.

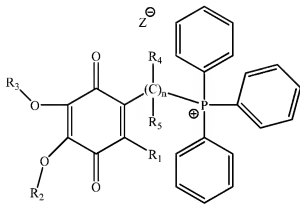
137. (Previously presented) The pharmaceutical composition of claim 135 wherein the pharmaceutically acceptable anion is selected from the group consisting of (i) an alkyl sulfonate, (ii) a pharmaceutically acceptable anion that is not a halogen ion, and (iii) a pharmaceutically acceptable anion that is not nucleophilic.

138. (Previously presented) The pharmaceutical composition of claim 135 wherein the pharmaceutically acceptable anion is selected from the group consisting of methanesulfonate, p-toluenesulfonate, ethanesulfonate, benzenesulfonate and 2-naphthalenesulfonate.

139. (Previously presented) The pharmaceutical composition of claim 135 wherein the pharmaceutically acceptable anion is methanesulfonate.

140. (Previously presented) The pharmaceutical composition of claim 135 wherein the antioxidant moiety is selected from the group consisting of (i) a quinone or a quinol, (ii) vitamin E, (iii) a chain breaking antioxidant, (iv) a fullerene, and (v) a spin trap.

141. (Previously presented) The pharmaceutical composition according to claim 135 wherein the compound has the general formula:



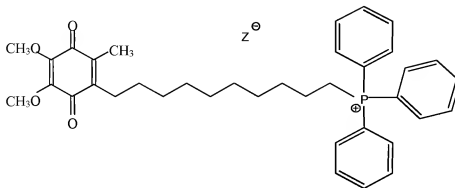
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or its quinol form, wherein R_1 , R_2 , and R_3 are the same or different and are selected from C_1 to C_5 alkyl, substituted C_1 to C_5 alkyl and H, wherein R_4 and R_5 are independently selected from the group consisting of H, hydroxyl, carboxyl, amide, unsubstituted or substituted alkyl, unsubstituted or substituted alkenyl and unsubstituted or substituted alkynyl, and wherein n is an integer from about 2 to 20, and wherein Z is a non-reactive anion.

142. (Previously presented) The pharmaceutical composition according to claim 141 wherein Z is selected from the group consisting of an alkyl sulfonate and an aryl sulfonate.

143. (Currently amended) The pharmaceutical composition according to claim 141 wherein C of $H(C)_n$ is saturated.

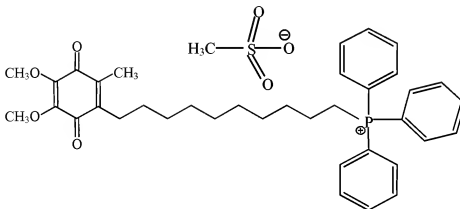
144. (Previously presented) The pharmaceutical composition according to claim 135 wherein the compound has the formula:



II

or its quinol form, wherein Z is the anionic complement.

145. (Previously presented) The pharmaceutical composition according to claim 135 wherein the compound has the formula:



(III).

146. (Previously presented) The pharmaceutical composition according to either claim 144 or claim 145 which comprises cyclodextrin.

147. (Previously presented) The pharmaceutical composition of claim 146 wherein the compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is from about 10:1 to about 1:10.

148. (Previously presented) The pharmaceutical composition of claim 146 wherein the compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is selected from the group consisting of (i) from about 5:1 to about 1:5, (ii) from about 4:1 to about 1:4, (iii) from about 2:1 to about 1:2, (iv) about 1:1 and (v) about 1:2.

149. (Previously presented) The pharmaceutical composition according to claim 146 wherein the cyclodextrin is β -cyclodextrin.

150. (Previously presented) The pharmaceutical composition according to claim 145 which comprises cyclodextrin wherein the compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is about 1:2.

151. (Previously presented) The pharmaceutical composition according to claim 135 that is selected from the group consisting of a pharmaceutical composition that is formulated for oral administration and a pharmaceutical composition that is formulated for parenteral administration.

152. (Previously presented) The pharmaceutical composition according to claim 145 which comprises cyclodextrin, and that is selected from the group consisting of a pharmaceutical composition that is formulated for oral administration and a pharmaceutical composition that is formulated for parenteral administration.

153. (Currently amended) A method of reducing oxidative stress in a cell, comprising:
contacting a cell that comprises mitochondria with a chemically stable antioxidant compound that comprises (i) a lipophilic cationic moiety linked by a linking moiety to an antioxidant moiety, and (ii) an anionic complement for said cationic moiety, wherein the cationic moiety is capable of mitochondrially targeting the antioxidant moiety, ~~and~~ wherein the anionic complement is a pharmaceutically acceptable anion that is not a halogen ion or a nitrate anion

and is selected from the group consisting of an alkyl sulfonate, an aryl sulfonate, tetrafluoroborate, trifluoromethanesulfonate, hexafluoroantimonate, hexafluoroarsenate, hexafluorophosphate, tetraphenylborate, and tetra(perfluorophenyl)borate, and does not exhibit reactivity against the antioxidant moiety, the cationic moiety or the linking moiety, and wherein the antioxidant compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity, under conditions and for a time sufficient for accumulation of the antioxidant compound in the mitochondria, and thereby reducing oxidative stress in the cell.

154. (Previously presented) The method of claim 153 wherein the lipophilic cationic moiety is a substituted or an unsubstituted triphenylphosphonium cation.

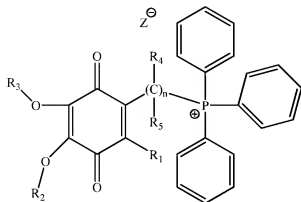
155. (Previously presented) The method of claim 153 wherein the pharmaceutically acceptable anion is selected from the group consisting of (i) an alkyl sulfonate, (ii) a pharmaceutically acceptable anion that is not a halogen ion, and (iii) a pharmaceutically acceptable anion that is not nucleophilic.

156. (Previously presented) The method of claim 153 wherein the pharmaceutically acceptable anion is selected from the group consisting of methanesulfonate, p-toluenesulfonate, ethanesulfonate, benzenesulfonate and 2-naphthalenesulfonate.

157. (Previously presented) The method of claim 153 wherein the pharmaceutically acceptable anion is methanesulfonate.

158. (Previously presented) The method of claim 153 wherein the antioxidant moiety is selected from the group consisting of (i) a quinone or a quinol, (ii) vitamin E (iii) a chain breaking antioxidant, (iv) a fullerene, and (v) a spin trap.

159. (Previously presented) The method of claim 153 wherein the compound has the general formula:



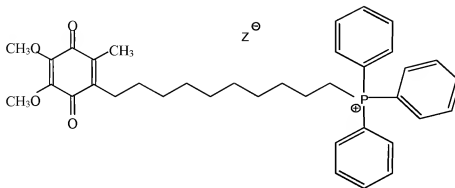
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or its quinol form, wherein R₁, R₂, and R₃ are the same or different and are selected from C₁ to C₅ alkyl, substituted C₁ to C₅ alkyl and H, wherein R₄ and R₅ are independently selected from the group consisting of H, hydroxyl, carboxyl, amide, unsubstituted or substituted alkyl, unsubstituted or substituted alkenyl and unsubstituted or substituted alkynyl, and wherein n is an integer from about 2 to 20, and wherein Z is a non-reactive anion.

160. (Previously presented) The method of claim 159 wherein Z is selected from the group consisting of an alkyl sulfonate and an aryl sulfonate.

161. (Previously presented) The method of claim 159 wherein C of I_n is saturated.

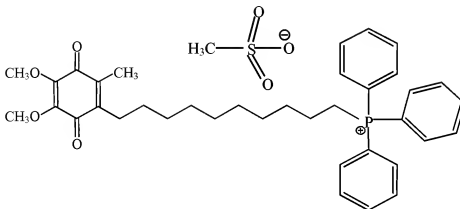
162. (Previously presented) The method of claim 153 wherein the antioxidant compound has the formula:



II

or its quinol form, wherein Z is the anionic complement.

163. (Previously presented) The method of claim 153 wherein the antioxidant compound has the formula:



(III).

164. (Previously presented) The method of either claim 162 or claim 163 wherein the antioxidant compound is present in a pharmaceutical composition that further comprises a carrier or excipient, wherein said carrier or excipient comprises cyclodextrin.

165. (Previously presented) The method of claim 164 wherein the antioxidant compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is from about 10:1 to about 1:10.

166. (Previously presented) The method of claim 164 wherein the compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is selected from the group consisting of (i) from about 5:1 to about 1:5, (ii) from about 4:1 to about 1:4, (iii) from about 2:1 to about 1:2, (iv) about 1:1 and (v) about 1:2.

167. (Previously presented) The method of claim 164 wherein the cyclodextrin is β -cyclodextrin.

168. (Previously presented) The method of claim 164 wherein the compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is about 1:2.

169. (Currently amended) A method of therapy of a patient who would benefit from reduced oxidative stress, comprising administering to said patient a therapeutically efficacious dose of a pharmaceutical composition which comprises (i) a chemically stable antioxidant compound that comprises a lipophilic cationic moiety linked by a linking moiety to an antioxidant moiety, (ii) an anionic complement for said cationic moiety, wherein the cationic moiety is capable of mitochondrially targeting the antioxidant moiety, ~~and~~ wherein the anionic complement is a pharmaceutically acceptable anion that is not a halogen ion or a nitrate anion and is selected from the group consisting of an alkyl sulfonate, an aryl sulfonate, tetrafluoroborate, trifluoromethanesulfonate, hexafluoroantimonate, hexafluoroarsenate, hexafluorophosphate, tetraphenylborate, and tetra(perfluorophenyl)borate, and does not exhibit reactivity against the antioxidant moiety, the cationic moiety or the linking moiety, and wherein the antioxidant compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity, and (iii) a carrier or excipient.

170. (Previously presented) The method of claim 169 wherein the lipophilic cationic moiety is a substituted or an unsubstituted triphenylphosphonium cation.

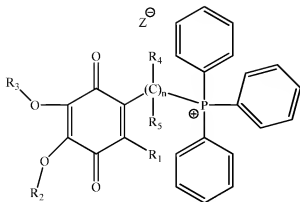
171. (Previously presented) The method of claim 169 wherein the pharmaceutically acceptable anion is selected from the group consisting of (i) an alkyl sulfonate, (ii) a pharmaceutically acceptable anion that is not a halogen ion, and (iii) a pharmaceutically acceptable anion that is not nucleophilic.

172. (Previously presented) The method of claim 169 wherein the pharmaceutically acceptable anion is selected from the group consisting of methanesulfonate, p-toluenesulfonate, ethanesulfonate, benzenesulfonate and 2-naphthalenesulfonate.

173. (Previously presented) The method of claim 169 wherein the pharmaceutically acceptable anion is methanesulfonate.

174. (Previously presented) The method of claim 169 wherein the antioxidant moiety is selected from the group consisting of (i) a quinone or a quinol, (ii) vitamin E, (iii) a chain breaking antioxidant, (iv) a fullerene, and (v) a spin trap.

175. (Previously presented) The method of claim 169 wherein the compound has the general formula:

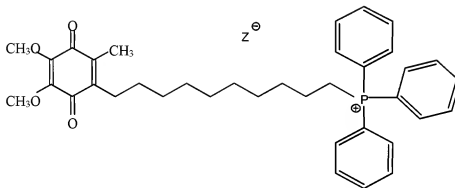


or its quinol form, wherein R_1 , R_2 , and R_3 are the same or different and are selected from C_1 to C_5 alkyl, substituted C_1 to C_5 alkyl and H, wherein R_4 and R_5 are independently selected from the group consisting of H, hydroxyl, carboxyl, amide, unsubstituted or substituted alkyl, unsubstituted or substituted alkenyl and unsubstituted or substituted alkynyl, and wherein n is an integer from about 2 to 20, and wherein Z is a non-reactive anion.

176. (Previously presented) The method of claim 175 wherein Z is selected from the group consisting of an alkyl sulfonate and an aryl sulfonate.

177. (Previously presented) The method of claim 175 wherein C of I_n is saturated.

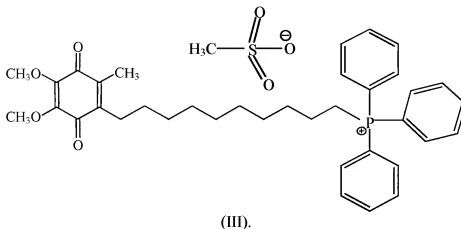
178. (Previously presented) The method of claim 169 wherein the antioxidant compound has the formula:



II

or its quinol form, wherein Z is the anionic complement.

179. (Previously presented) The method of claim 169 wherein the antioxidant compound has the formula:



180. (Previously presented) The method of either claim 178 or claim 179 wherein the carrier or excipient comprises cyclodextrin.

181. (Previously presented) The method of claim 180 wherein the compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is from about 10:1 to about 1:10.

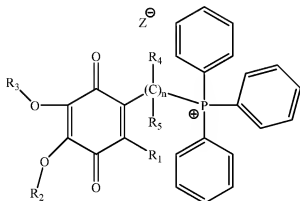
182. (Previously presented) The method of claim 180 wherein the compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is selected from the group consisting of (i) from about 5:1 to about 1:5, (ii) from about 4:1 to about 1:4, (iii) from about 2:1 to about 1:2, (iv) about 1:1 and (v) about 1:2.

183. (Previously presented) The method of claim 180 wherein the cyclodextrin is β -cyclodextrin.

184. (Previously presented) The method of claim 180 wherein the compound and cyclodextrin are present at a compound-to-cyclodextrin molar ratio that is about 1:2.

185. (Previously presented) The method of claim 169 wherein the step of administering comprises administration that is selected from oral administration and parenteral administration.

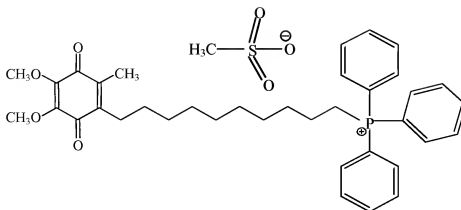
186. (Currently amended) A method of preparing an antioxidant compound that is capable of reducing oxidative stress in a cell, comprising admixing cyclodextrin or a cyclodextrin derivative that is selected from β -cyclodextrin, sulfobutylcyclodextrin, maltosylcyclodextrin, and hydroxypropylcyclodextrin, with a compound of the formula I



I

or its quinol form, wherein R₁, R₂, and R₃ are the same or different and are selected from C₁ to C₅ alkyl, substituted C₁ to C₅ alkyl and H, wherein R₄ and R₅ are independently selected from the group consisting of H, hydroxyl, carboxyl, amide, unsubstituted or substituted alkyl, unsubstituted or substituted alkenyl and unsubstituted or substituted alkynyl, wherein n is an integer from 2 to 20, and wherein Z is a pharmaceutically acceptable anion that is not a bromide ion or a nitrate anion and does not exhibit reactivity against any moiety of the compound of formula I, and wherein the compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity.

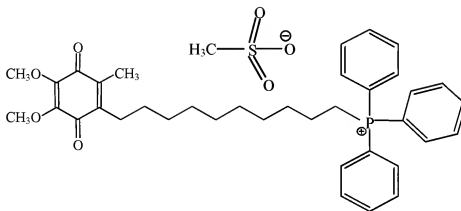
187. (Currently amended) A method of preparing an antioxidant compound that is capable of reducing oxidative stress in a cell, comprising admixing cyclodextrin or a cyclodextrin derivative that is selected from β -cyclodextrin, sulfobutylcyclodextrin, maltosylcyclodextrin, and hydroxypropylcyclodextrin, with a compound having the formula:



(III)

or its quinol form, wherein the compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity.

188. (Currently amended) A method of synthesis of a compound having the formula



(III),

or its quinol form, said method comprising reacting idebenol mesylate with triphenylphosphine, wherein the compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity.

189. (Previously presented) The method of claim 188 which comprises chemically reducing idebenone mesylate to obtain idebenol mesylate prior to the step of reacting the idebenol mesylate with triphenylphosphine.

190. (Previously presented) The method of claim 188 further comprising, prior to the reaction of idebenone mesylate with triphenylphosphine, the steps of:

- (a) adding triethylamine to an idebenone solution to obtain an idebenone triethylamine mixture;
- (b) cooling the idebenone triethylamine mixture of (a); and
- I reacting the idebenone triethylamine mixture with a methanesulfonyl chloride solution to obtain idebenone mesylate.

191. (Previously presented) The method of claim 190 comprising at least one of:

- (i) step (a) wherein adding triethylamine comprises adding a molar excess of triethylamine relative to idebenone,
- (ii) step (b) wherein cooling comprises cooling to $10\pm 3^{\circ}\text{C}$, and
- (iii) step I wherein reacting comprises reacting at approximately $10\text{--}15^{\circ}\text{C}$.

192. (Currently amended) A pharmaceutical composition suitable for treatment of a patient suffering from or predisposed to Parkinson's disease, Alzheimer's disease, Huntington's Chorea, or Friedreich's Ataxia, which comprises an effective amount of an antioxidant compound which comprises a lipophilic cationic moiety linked by a linking moiety to an antioxidant moiety, and an anionic complement for said cationic moiety, wherein the cationic moiety is capable of mitochondrially targeting the antioxidant moiety, ~~and~~ wherein the anionic complement is a pharmaceutically acceptable anion that is not a halogen ion or a nitrate anion and is selected from the group consisting of an alkyl sulfonate, an aryl sulfonate, tetrafluoroborate, trifluoromethanesulfonate, hexafluoroantimonate, hexafluoroarsenate, hexafluorophosphate, tetraphenylborate, and tetra(perfluorophenyl)borate, and does not exhibit reactivity against the antioxidant moiety, the cationic moiety or the linking moiety; and a carrier or excipient, and wherein the antioxidant compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity.

193. (Currently amended) A method of therapy of a patient suffering from or predisposed to Parkinson's disease, Alzheimer's disease, Huntington's Chorea, or Friedreich's Ataxia which comprises the step of administering to said patient an antioxidant compound that comprises (i) a lipophilic cationic moiety linked by a linking moiety to an antioxidant moiety, and (ii) an anionic complement for said cationic moiety, wherein the cationic moiety is capable of mitochondrially targeting the antioxidant moiety, ~~and~~ wherein the anionic complement is a pharmaceutically acceptable anion that is not a halogen ion or a nitrate anion and is selected from the group consisting of an alkyl sulfonate, an aryl sulfonate, tetrafluoroborate, trifluoromethanesulfonate, hexafluoroantimonate, hexafluoroarsenate, hexafluorophosphate, tetraphenylborate, and tetra(perfluorophenyl)borate, and does not exhibit reactivity against the antioxidant moiety, the cationic moiety or the linking moiety, and wherein the antioxidant compound exhibits less than 10% decomposition after 60 days at 25°C, 50% relative humidity.